In the claims:

Please amend claim 31 as follows:

All the pending claims are set forth below for the convenience of the Examiner

1. **(Amended)** A method for [selectively] inhibiting proliferation of [a] hematopoietic cells engineered *ex vivo* to express [comprising contacting a hematopoietic cell which ectopically expresses] a gene encoding a mutated macrolide binding protein (MBP), which method comprises contacting the cells with a macrolide which [selectively] induces macrolide-dependent inhibition of proliferation of the cells [expressing the mutated MBP compared to cells expressing a wild-type form of the MBP, the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP].

2. **(Amended)** A method for selectively inhibiting proliferation of a hematopoietic cell comprising

   (i) causing[, in] the cell[, the ectopic expression of] to express an MBP gene encoding a mutated macrolide binding protein (MBP) having an altered macrolide-binding specificity relative to a wild-type form of the MBP, which mutated MBP retains the ability to cause macrolide-dependent inhibition of proliferation; and

   (ii) contacting the cell with a macrolide which selectively binds to the altered MBP relative to the wild-type MBP and selectively induces macrolide-dependent inhibition of proliferation of cells expressing the mutated MBP relative to cells not expressing [only] the wild-type MBP.

3. **(Amended)** The method of claim 1 or 2, wherein the MBP is selected from the group consisting of a FRAP, an FK506-binding protein, a cyclophilin and a calcineurin.

4. **(Amended)** The method of claim 1 or 2, wherein the mutated MBP has a dissociation constant, K_d, at least one order of magnitude less than the K_d of the wild-type MBP.

5. **(Amended)** The method of claim 4 [2], wherein the mutated MBP has a dissociation constant, K_d, at least three orders of magnitude less than the K_d of the wild-type MBP.

6. **(Amended)** The method of claim 1 or 2, wherein the MBP gene is present on an expression vector in the cell.

7. **(Amended)** The method of claim 1 or 2, wherein the MBP gene is present in the cell as part of a viral expression construct.

8. **(Amended)** The method of claim 1 or 2, wherein the MBP gene is a homologous recombinant in the cells genomic DNA.

9. **(Amended)** The method of claim 1 or 2, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.

10. **(Amended)** The method of claim 1 or 2, wherein the MBP gene encodes a FRAP protein, and the macrolide is an analog of rapamycin.

11. **(Amended)** The method of claim 1 or 2, wherein the MBP gene encodes an FK506 binding protein, and the macrolide is an analog of FK506 or rapamycin.

12. **(Amended)** The method of claim 1 or 2, wherein the MBP gene encodes a calcineurin protein, and the macrolide is an analog of FK506 or cyclosporin.

13. **(Amended)** The method of claim 1 or 2, wherein the MBP gene encodes a cyclophilin protein, and the macrolide is an analog of cyclosporin.

14. **(Amended)** The method of claim 1 or 2, wherein the cell is a mammalian cell.

15. **(Amended)** The method of claim 1 or 2, wherein the cell is a human cell.

16. (**amended**) A method for selectively inhibiting proliferation of a transplanted hematopoietic cell comprising

(i) transplanting, into an animal, hematopoietic cells which have been engineered to express [ectopically expresses] a MBP gene encoding a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP

(ii) administering to the animal an amount of a macrolide sufficient to inhibit proliferation of the transplanted cells, which macrolide selectively induces macrolide-dependent inhibition of proliferation of cells expressing the mutated MBP compared to cells expressing a wild-type form of the MBP.

17. The method of claim 16, wherein the MBP is selected from the group consisting of a FRAP, an FK506-binding protein, a cyclophilin and a calcineurin.

18. The method of claim 16, wherein the mutated MBP has a dissociation constant, K_d, at least one order of magnitude less than the K_d of the wild-type MBP.

19. The method of claim 16, wherein the mutated MBP has a dissociation constant, K_d, at least three orders of magnitude less than the K_d of the wild-type MBP.

20. The method of claim 16, wherein the MBP gene is present on an expression vector in the cell.

21. The method of claim 16, wherein the MBP gene is present in the cell as part of a viral expression construct.

22. The method of claim 16, wherein the MBP gene is a homologous recombinant in the cells genomic DNA.

23. The method of claim 16, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.

24. The method of claim 16, wherein the animal is a mammal.

25. The method of claim 24, wherein the animal is a human.

26. The method of claim 16, wherein the transplanted cells are autologous to the animal.

27. The method of claim 16 or 26, wherein the transplanted cells comprise transplanted bone marrow.

28. The method of claim 16 or 26, wherein the transplanted cells comprise hematopoietic stem cells.

29. The method of claim 16, wherein the ectopic expression of the MBP gene is transcriptionally regulated by a T-cell specific transcriptional regulatory sequence.

30. The method of claim 16, wherein the animal is in an immunosuppressed state.

31. **(Amended)** A method for [treating] <u>reducing</u> graft-versus-host disease in ~~an animal~~ by selectively inhibiting proliferation of <u>a</u> transplanted hematopoietic ~~cell~~[s], comprising

(i) prior to transplanting tissue containing <u>a</u> hematopoietic cell[s], transducing [at least a sub-population of] <u>the</u> hematopoietic ~~cell~~[s] [of the tissue] with a gene for ectopic expression of a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP; and

(ii) subsequent to transplanting the hematopoeitic cell[s], administering to the animal an amount of a macrolide sufficient to inhibit proliferation of the hematopoeitic transplanted

cell[s], which macrolide selectively induces macrolide-dependent inhibition of proliferation of the transplanted cell[s] expressing the mutated MBP compared to endogenous cells of the animal.

32. An expression construct encoding a mutated macrolide binding protein (MBP) selected from the group consisting of FRAP, FKBP, cyclophilin and calcineurin, wherein the mutated MBP has an altered macrolide-binding specificity relative to the wild-type form MBP and, in the presence of a macrolide which binds the mutated MBP, induces macrolide-dependent inhibition of proliferation of a cell expressing the mutated MBP.

33. A kit for for selectively inhibiting proliferation of a hematopoietic cell, comprising

(i) an expression construct for ectopically expressing an MBP gene encoding a mutated macrolide binding protein (MBP) having an altered macrolide-binding specificity relative to a wild-type form of the MBP, which mutated MBP retains the ability to cause macrolide-dependent inhibition of proliferation; and

(ii) a macrolide which selectively binds to the altered MBP relative to the wild-type MBP and selectively induces macrolide-dependent inhibition of proliferation of cells expressing the mutated MBP relative to cells not expressing only the wild-type MBP.

34. A method of promoting engraftment and hematopoietic activity of a hematopoietic stem cell from a donor, comprising:

(a) inserting nucleic acid encoding a modified macrolide binding protein specific for a modified macrolide into a hematopoietic stem cell to produce a transformed hematopoietic stem cell;

(b) introducing the transformed hematopoietic stem cell into a recipient mammal, such that the modified cellular receptor cyclophilin is expressed; and,

(c) administering an effective amount of the modified cyclosporin to said recipient mammal.

35. Hematopoietic stem cells transfected with the expression construct of claim 32.

36. A T cell transfected with an expression construct of claim 32.

37. **(new)** A method for rendering a hematopoietic cell susceptible to inhibition by a modified macrolide, comprising transfecting isolated hematopoietic cells *ex vivo* with the construct of

claim 32

38. **(new)** A method for rendering a hematopoietic cell susceptible to inhibition by a modified macrolide, comprising transfecting isolated hematopoietic cells *ex vivo* with a nucleic acid having a coding sequence for a polypeptide consisting essentially of a modified macrolide binding protein (MBP) having an altered macrolide-binding specificity relative to a wild-type form of the MBP, which mutated MBP retains the ability to cause macrolide-dependent inhibition of proliferation of the cell.

39. **(new)** The method of claim 38, comprising the further step of introducing the transfected hematopoietic cell into a recipient mammal.

40. **(new)** The method of claim 2, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

41. **(new)** The method of claim 3, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

42. **(new)** The method of claim 4, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

43. **(new)** The method of claim 9, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

Remarks

Claims 1-43 are pending. Applicants note with appreciation that claims 1-36 were found to be free of the art. Support for the amendment to claim 31 can be found at page 38, line 30. No new matter has been added.

Cancellation and/or amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The cancellation and/or amendments to the claims are being made solely to expedite prosecution of one set of claims to subject matter of potential clinical and/or commercial significance. Applicants reserve the option to further prosecute additional claims, including without limitation claims of the same or similar scope as the claims originally filed in the instant patent application.